

Case reports

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De novo direct tandem duplication of the proximal long arm of chromosome 2: 46,XX,dir dup(2)(q11·2q14·2)

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SUMMARY A child is described with a de novo direct duplication of the region 2q11·2→2q14·2. She probably represents the first reported case of proximal 2q duplication. The abnormalities included short stature, microcephaly, brachycephaly, depressed nasal bridge, prominent philtrum, congenital glaucoma, and mental retardation.

Duplication of the proximal long arm of chromosome 2 has not been previously reported. In this paper, we report a de novo direct duplication of the proximal segment of chromosome 2 (q11·2→q14·2) in a 3½-year-old girl with mental retardation and dysmorphic features, including congenital glaucoma.

Case report

The proband, a 3½-year-old Mexican-American girl, was the first child born to a 22-year-old father and a 21-year-old mother. Her birth weight after a 40 week gestation was 2850 g and her head circumference was 32·7 cm (5th centile). She had a normal 1-year-old sister. The family history and the antenatal history were unremarkable. Specifically, there was no history of exposure to potential mutagens or teratogens before or during the pregnancy in either parent.

She was diagnosed as having congenital glaucoma. Her development in the first year of life was delayed. She rolled over at 4 months, sat unsupported at 12 months, and walked at 16 months. At 38 months her developmental levels were: gross motor 15 to 21 months, fine motor 15 to 21 months, social skills 27 to 33 months, and self-help skills 15 to 21 months.

On physical examination at 3½ years of age, her weight was 12 kg and her height was 89 cm (below the 5th centile). Her skull was microcephalic

(44·5 cm) and brachycephalic. She had a depressed nasal bridge and her nasal septum was prominent and extended below the level of the nares. Her philtrum was also prominent (fig 1). She had mild clinodactyly but had no shortening of the fourth metacarpal bones. Her deep tendon reflexes were sluggish and muscle tone was decreased. She expressed no intelligible vocabulary.

CYTOGENETIC STUDIES

Peripheral blood and skin fibroblast cells were cultured and the chromosomes GTG banded using standard techniques. One chromosome 2 had two extra dark bands in the proximal long arm, which appeared to be a tandem duplication of bands q11·2→q14·2 (fig 2). From the banding pattern, we could not distinguish with certainty whether the duplication was direct or inverted. However, we reasoned that it was more likely to be direct because neither breakpoint was near the end of the chromosome; by contrast, in almost all reported inverted duplications, one breakpoint is terminal or nearly



FIG 1 The proband.

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FIG 2 Chromosome 2 pairs from the proband, depicting the duplication of 2q11-2→2q14-2.

terminal.¹ The proband's karyotype was therefore designated as 46,XX,dir dup(2)(q11-2q14-2). Both parents had normal peripheral blood karyotypes, so the duplication was considered to be de novo.

Discussion

A duplication of the proximal long arm of chromosome 2 has not been previously reported. The chromosome abnormality appears to have caused the mild dysmorphic features and the mental retardation. The only unusual feature we observed was congenital glaucoma. However, delineation of a 'proximal 2q duplication syndrome' may be possible when other cases are described.

The parental age in this case is consistent with the observation that direct duplications are not

associated with advanced parental age¹ and may arise from unequal crossing over during gametogenesis. We are unaware of any instance of recurrence or inheritance of an autosomal direct duplication. Two inherited duplications of the X chromosome have been reported, but with minor or no physical effects in the carrier females.^{2,3} The risk of recurrence is probably low but unknown and therefore antenatal diagnosis is an option in future pregnancies.

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First trimester fetal karyotyping in twin pregnancy

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SUMMARY Fetal chromosome analysis in a twin pregnancy during the first trimester is described. Problems of the reliability of tissue sampling are also discussed. The authors emphasise the advantage of direct cytogenetic analysis from the tissue specimens used for enzyme determination or DNA studies.

The discovery of twins at the time of fetal diagnosis complicates the counselling problem; for example, it alters the risk of finding an affected fetus or the

twins may be discordant for the abnormality.¹ Moreover, the inability to test both twins may occur and diagnostic procedures which are reliable in a singleton pregnancy may not be so in a twin pregnancy. We present our first experience of fetal chromosome analysis of twins during the first trimester and emphasise the importance of obtaining reliable samples from each twin.

Case report

The proband, a 42-year-old G9 P6 woman, was referred to us because of advanced maternal age. At 9 weeks' gestation ultrasound examination